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A simple tool to predict exercise capacity of obese patients with ischaemic heart disease

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Objective: To define an equation that predicts exercise capacity taking into account body mass index (BMI).
Design: Retrospective analysis and validation study of a multidisciplinary programme aimed at weight loss and physical rehabilitation.
Setting: Tertiary referral hospital.
Patients and methods: 372 consecutive obese participants (249 men) with stable ischaemic heart disease, aged mean 60.1 (SD 8.7) years, underwent a treadmill exercise test. BMI was 37.8 (4.5) kg/m^2. In the validation study the model was tested in 87 patients with similar characteristics.
Results: Mean exercise intensity was 6.6 (SD 2.4) metabolic equivalents (METs). Multivariate linear regression analysis defined two simple models that considered exercise intensity as the dependent variable and a set of independent variables such as anthropometric measures, age and sex in the first one, plus associated clinical conditions and drug treatment in the second one. The correlation coefficients of the two models were $R = 0.630$ and $R = 0.677$, respectively. Age, BMI and sex were the strongest predictors of exercise capacity. The first derived equation efficiently predicted exercise capacity: in the validation study predicted exercise intensity was 6.3 (1.6) METs and attained exercise intensity was 6.3 (2.4) METs ($p = 0.903$) with a highly significant correlation ($R = 0.534$, $p < 0.001$).
Conclusion: BMI is an important determinant of exercise capacity of obese people with ischaemic heart disease. The use of a simple equation may help in predicting exercise capacity, in individualising exercise protocol and in setting up rehabilitation programs for obese patients.

The prevalence of obesity is increasing in the Western world. Diet and exercise remain the cornerstone of treatment, especially in the subset of patients who have cardiovascular diseases.[1 2] Obesity is associated with all the conventional risk factors for ischaemic heart disease (IHD), as well as with novel risk factors,[3] and is an independent risk factor for IHD.[4] Moreover, obese patients are at higher risk of developing congestive heart failure.[5]

Exercise tolerance is a very strong marker of survival in unselected populations, as well as in patients with coronary heart disease.[6–9] Although we lack data specifically from the obese population, this marker probably also has meaningful predictive value in this kind of patient. Obese patients rarely achieve the recommended levels of exercise, independently of their clinical status, since obesity reduces exercise capacity.[10] The cardiorespiratory parameters defined in normal weight populations differ to some degree for the obese population, and this has implications for optimising exercise intensity for weight loss and rehabilitation programmes for obese adults.[11] This underscores the need for a more accurate definition of the reference values in the subset of obese patients.

Specific tables used to predict exercise capacity of the obese population have not been defined: the commonly used ones have been studied in population samples that include a large number of non-obese participants, and very sedentary people such as those who are obese may have difficulty answering the specific activity questionnaire.[12 13] We are not aware of any study that has tried to predict exercise tolerance in a population composed only of obese participants.

The purpose of our study was to define a simple equation that can help predict the level of exercise taking into account body mass index (BMI) along with other easily obtainable variables. This will be useful in defining exercise test protocols, establishing rehabilitation programmes and programming follow-up studies of the prognostic value of exercise testing in obese participants with IHD.

PATIENTS AND METHODS

Retrospective analysis

We retrospectively analysed 372 consecutive white patients (249 men) with IHD and obesity (mean BMI 37.8 (SD 4.5) kg/m^2, range 30.0–52.1) kg/m^2) who underwent a symptom limited exercise stress test to define their effort tolerance for exercise prescription in the setting of a multidisciplinary program aimed at weight loss and physical rehabilitation. IHD was defined as a history of at least one of the following: myocardial infarction, coronary artery bypass grafting and percutaneous transluminal coronary angioplasty. Patients with recent (within less than two months) myocardial infarction, coronary artery bypass or coronary angioplasty were excluded. Patients with orthopaedic limitations were also excluded. All patients were clinically stable and none had clinically evident heart failure according to the Framingham criteria.[14] The study was conducted at the San Giuseppe Hospital, Piancavallo, Italy.

Validation analysis

After defining the equation we verified its ability to predict the exercise capacity of 87 patients with the same characteristics as the population described above in terms of age, BMI, height and sex distribution. All the patients had a diagnosis of IHD (based on the same criteria that we used for the population selected for the retrospective analysis) and were

Abbreviations: BMI, body mass index; IHD, ischaemic heart disease; METs, metabolic equivalents; QUICKI, quantitative insulin sensitivity check index

clinically stable without symptoms of congestive heart failure.

Exercise test protocol

Exercise tests were conducted in the morning. Patients had breakfast at least two hours before exercising and assumed their regular drugs. Each patient gave informed written consent to the test. We used a Marquette series 2000 motorised treadmill together with Marquette Max Personal ECG instrumentation (Marquette Medical Systems, Milwaukee, Wisconsin, USA). We measured the intensity of exercise as metabolic equivalents (METs). We derived our estimate of METs from treadmill speed and grade. We used a ramp protocol that took into consideration that many obese patients are unable to start exercise at a treadmill speed greater than 2 km/h.[15 16] Moreover, we needed a protocol that could describe very low grades of effort tolerance, considering that in our experience about 15% of patients tolerate and intensity of less than 4 METs. The initial speed of the treadmill was 1.5 km/h and was increased regularly by 0.3 km/h/min. The initial inclination was 0% and was increased progressively by one grade every minute. Blood pressure was checked manually at baseline, every two minutes during exercise, at peak effort, at the end of the first minute of recovery and then again every two minutes. ECG and heart rate were constantly monitored. An ECG strip (12 leads) was printed at baseline, and heart rate and PR, QRS and QT intervals were automatically measured. QT interval corrected for heart rate was calculated by Bazett's formula. ECG strips were printed every two minutes and at peak effort. During recovery (which lasted at least five minutes) the ECG was printed at the end of the first minute and then again every two minutes. Patients were encouraged to continue exercising until symptoms limited further continuation even after reaching 85% of their maximum predicted heart rate. Reasons for test termination were limiting symptoms (fatigue, angina, dyspnoea and muscular pain), abnormal ECG, abnormal blood pressure or by the patient's choice.

Other tests

Patients were examined echocardiographically for the calculation of ejection fraction. Two dimensional and two dimensionally directed M mode echocardiographic measurements were obtained with a Vingmed System 5 instrument (GE Medical Systems, Milwaukee, Wisconsin, USA). Parasternal long and short axis views and apical two and four chamber views were used to evaluate left ventricular and valvar function with a multifrequency sector transducer set on ideal frequency to obtain optimal imaging. Depending on the quality of the images ejection fraction was calculated with the two dimensional (Simpson) or M mode method (Teichholz).[17 18] Blood samples from each patient were also examined for lipids, glucose, insulin and fibrinogen before the exercise stress test. Insulin sensitivity was calculated by the quantitative insulin sensitivity check index (QUICKI), which has been validated for obese subjects,[19] by the method of Katz *et al*.[20] Insulin and QUICKI were analysed only for non-diabetic patients and for diabetics taking oral drugs; patients treated with insulin were not considered.

The study was approved by our institutional ethics committee.

Statistical analysis

Continuous data are presented as mean (SD) and categorical variables are presented as number and percentage. Male sex was coded as 1 and female sex as 0. For drug treatment and associated clinical conditions the presence of the variable was coded as 1 and the absence as 0.

A simple linear regression was executed with exercise intensity in METs as the dependent variable with all the continuous variables. A two sided t test for unpaired variables was calculated to study the difference in exercise intensity attained for categorical variables. A χ^2 test was calculated when appropriate; p values were calculated by two tailed Fisher's exact test. Variables that were significantly related (at the level of $p < 0.05$) to the dependent variable (exercise intensity) were used in a multiple linear regression model. Criteria for inclusion and exclusion in the stepwise regression were probability of F to enter $\leqslant 0.050$ and probability of F to remove $\geqslant 0.100$. Partial correlation with the dependent variable was assessed after controlling for age, BMI and sex—that is, the variables that more powerfully predicted exercise capacity.

Data were statistically analysed with the SPSS V.10.1 package (SPSS, Chicago, Illinois, USA).

RESULTS

Associated clinical conditions were hypertension in 252 patients (68%), atrial fibrillation in 14 (4%) and diabetes in 104 (28%). Forty patients (38% of diabetic patients) were taking insulin and 64 were taking oral drugs. Two hundred and sixty eight patients (72%) were classified as having metabolic syndrome as defined by Adult Treatment Panel III criteria.[21] One hundred (27%) patients were current smokers. Table 1 summarises the baseline characteristics of the study population.

No patients experienced adverse effects during the exercise stress test. Mean exercise intensity was 6.6 (SD 2.4) METs (range 1.5–15.4) METs). The perceived exertion on the 20 point Borg scale was 13.9 (1.8).

Several variables differed significantly between women and men: men were younger and taller, and had lower BMI, higher waist circumference, lower systolic blood pressure, lower resting heart rate, lower total and high density lipoprotein cholesterol, higher triglycerides and a lower insulin sensitivity index. Women reached a significantly lower level of exercise: 5.4 (1.9) *v* 7.2 (2.5) METs ($p < 0.001$). One hundred and three women (84%) and 202 men (81%) had reduced exercise capacity considering the reference values that were recently proposed by Aktas and colleagues.[22] Mean test duration was 489 (SD 187) seconds (or eight minutes and nine seconds) and 220 patients (59%) exercised for a time between 6 and 12 minutes, thus approximating the test duration that is considered optimal.[23 24] It is worth noting that the vast majority of female patients whose exercise duration fell outside the desired limits exercised less than 6 minutes and only 2% exercised longer than 12 minutes. This trend was not evident for men.

Seventy patients stopped the exercise test because they had chest pain. These patients reached a lower level of exercise (5.4 (2.0) *v* 6.9 (2.4) METs, $p < 0.001$). Sixty nine per cent of patients who experienced chest pain were treated with glyceryl trinitrate (GTN) whereas only 7% of patients who did not have chest pain were treated with GTN ($p < 0.001$). Even if angina was a posteriori highly related to exercise capacity, anamnesis of angina was only a weak predictor of exercise capacity in univariate analysis ($p = 0.041$). Indeed some patients who experienced angina during exercise stress test did not report chest pain in everyday activities whereas some of the patients who reported angina did not have it during the test.

Most patients had normal or mildly reduced left ventricular function: ejection fraction was lower than 0.40 in 60 patients (16%), 0.40–0.55 in 152 (41%) and greater than 0.55 in 160 (43%).

By doing a simple linear regression analysis we looked for continuous variables that were related to attained METs.

Table 1 Baseline characteristics of patients and difference between men and women

	Overall	Women	Men	p Value
Cholesterol (mmol/l)	5.15 (1.19)	5.39 (1.04)	5.05 (1.24)	0.015
HDL (mmol/l)	1.14 (0.31)	1.32 (0.31)	1.04 (0.26)	< 0.001
LDL (mmol/l)	3.11 (0.93)	3.21 (0.88)	3.03 (1.09)	0.109
Triglycerides (mmol/l)	2.05 (1.16)	1.82 (1.15)	2.16 (1.16)	0.009
Fibrinogen (mmol/l)	11.11 (2.50)	11.41 (2.32)	10.97 (2.59)	0.193
Glucose (mmol/l)	6.38 (2.17)	6.49 (2.05)	6.33 (2.22)	0.732
Insulin (pmol/l)	93.8 (56)	83.3 (42)	98.6 (60)	0.117
QUICKI	0.3240 (0.0248)	0.3300 (0.0263)	0.3213 (0.0238)	0.044
Age (years)	60.1 (8.7)	62.0 (9.2)	59.1 (8.4)	0.002
BMI (kg/m^2)	37.7 (4.5)	38.6 (4.6)	37.3 (4.4)	0.009
Waist (cm)	116 (9)	109 (7)	119 (7)	<0.001
Height (m)	1.65 (0.09)	1.56 (0.07)	1.70 (0.07)	<0.001
Systolic BP (mm Hg)	122 (18)	125 (21)	121 (16)	0.029
Diastolic BP (mm Hg)	75 (9)	76 (10)	75 (9)	0.501
Resting HR (beats/min)	71 (13)	73 (13)	70 (12)	0.037

Data are mean (SD).
BMI, body mass index; BP, blood pressure; HDL, high density lipoprotein; HR, heart rate; LDL, low density lipoprotein; QUICKI, quantitative insulin sensitivity check index.
Reference values: for blood lipid concentrations see Adult Treatment Panel III criteria[21]; normal fibrinogen 6.88–11.8 μmol/l; glucose 3.33–6.11 mmol/l; insulin 13.9–201 pmol/l; QUICKI 0.335–0.365.

Ejection fraction was not related to exercise capacity ($r = 0.090$, $p = 0.086$), whereas several biochemical parameters were univariately related to attained exercise intensity: high density lipoprotein ($r = -0.190$, $p < 0.001$), triglycerides ($r = 0.178$, $p = 0.001$), fibrinogen ($r = -0.281$, $p < 0.001$) and QUICKI ($r = 0.166$, $p = 0.040$).

Since our main purpose was to produce an equation that can be used in everyday practice, we chose to define a model that uses only variables that are always available before the beginning of a standard exercise test. Moreover, we preferred to include only objective measurements and to avoid symptoms that can sometimes be misleading: we therefore excluded a history of angina from the variables entered in the multivariate model and we considered only anthropometric measures, age, sex, associated clinical conditions, heart rate, blood pressure and pharmacological treatment. Various baseline characteristics were significantly related to exercise intensity in univariate analysis: age, height, BMI, systolic blood pressure and heart rate. Table 2 shows correlations with continuous variables.

We also calculated the difference in attained exercise intensity by unpaired t test for dichotomic variables such as sex, drug treatment and associated clinical conditions. Table 3 shows the results.

Among clinical conditions the presence of diabetes and atrial fibrillation was associated with a lower level of exercise. Among treatments the use of β blockers and antiplatelet drugs was associated with a higher level of exercise, whereas the use of diuretics, digoxin and GTN was associated with a lower level of exercise. Interestingly atrial fibrillation was associated with a higher use of diuretics and digoxin: 86% of

Table 2 Correlations between exercise capacity, age, anthropometric measures, blood pressure and ECG intervals

Variable	*R*	p Value
Age	−0.469	<0.001
Height	0.375	<0.001
Weight	0.022	0.667
BMI	−0.319	<0.001
Waist	−0.043	0.412
Systolic BP	−0.186	<0.001
Diastolic BP	−0.053	0.533
HR	−0.199	<0.001
PR interval	0.049	0.476
QTc	−0.002	0.955
QRS interval	−0.014	0.839

BMI, body mass index; BP, blood pressure; HR, heart rate; QTc, QT interval corrected for HR.

Table 3 Differences in exercise capacity with respect to sex, associated clinical conditions, smoking habit and drug treatment

Variable		No	Exercise capacity (METs)	p Value
Sex	Men	249	7.2 (2.5)	<0.001
	Women	123	5.4 (1.9)	
Hypertension	No	120	6.8 (2.6)	0.221
	Yes	252	6.5 (2.3)	
Atrial fibrillation	No	358	6.7 (2.4)	0.002
	Yes	14	4.7 (2.0)	
Metabolic syndrome	No	72	6.2 (2.4)	0.284
	Yes	268	6.7 (2.5)	
Diabetes	No	268	6.8 (2.5)	0.040
	Yes	104	6.2 (2.3)	
Smoking habit	No	290	6.5 (2.3)	0.770
	Yes	82	6.6 (2.8)	
β Blockers	No	121	6.1 (2.5)	0.003
	Yes	251	6.9 (2.3)	
Diuretics	No	193	7.5 (2.4)	< 0.001
	Yes	179	5.7 (2.1)	
ACE inhibitors	No	150	6.6 (2.5)	0.728
	Yes	222	6.6 (2.4)	
Calcium channel blockers (dihydropyridine)	No	292	6.7 (2.4)	0.111
	Yes	80	6.2 (2.4)	
Calcium channel blockers (benzothiazepines)	No	332	6.7 (2.4)	0.126
	Yes	40	6.0 (2.5)	
ARB	No	316	6.7 (2.4)	0.068
	Yes	56	6.0 (2.3)	
Antiplatelet	No	52	6.0 (2.2)	0.039
	Yes	320	6.7 (2.5)	
Anticoagulant	No	331	6.6 (2.5)	0.282
	Yes	41	6.2 (2.2)	
Digoxin	No	358	6.7 (2.4)	0.006
	Yes	14	4.9 (2.2)	
Arrhythmia drug	No	354	6.3 (2.5)	0.578
	Yes	18	6.6 (2.4)	
Glyceryl trinitrate	No	262	7.0 (2.5)	< 0.001
	Yes	110	5.6 (2.0)	
Lipid lowering drug	No	128	6.7 (6.7)	0.377
	Yes	244	6.5 (2.3)	
α Blocker	No	355	6.6 (2.4)	0.700
	Yes	17	6.8 (2.60	

ACE, angiotensin converting enzyme; ARB, angiotensin receptor blocker; METs, metabolic equivalents.

patients with versus 53% of patients without atrial fibrillation were taking diuretics ($p = 0.005$), and 57% of patients with versus 2% of patients without atrial fibrillation were taking digoxin ($p < 0.001$).

We investigated the possibility that a multivariate linear model would be able to satisfactorily predict exercise tolerance by combining the variables that were related to exercise capacity in the univariate analysis. The first step in the definition of the model was a stepwise linear regression that considered age, BMI, sex and height. All the variables were kept in the model ($R = 0.630$). The standard error of the estimate is 1.899. The equation we derived was the following: exercise capacity (METs) = 14.53 − (0.12 × age) − (0.17 × BMI) + (3.16 × height) (+ 0.71 for male patients). In fig 1 we plotted the exercise intensity predicted by this equation versus that attained.

The second step consisted of a two-layer linear regression. We decided to force into the first layer of the regression, in addition to age, BMI and sex, the patient's height, which contributes slightly to the prediction of exercise capacity. In the second layer of the regression we used a set of other variables chosen from those that were statistically related to effort tolerance in univariate analysis—that is, heart rate, systolic blood pressure, atrial fibrillation, diabetes and treatment with β blockers, diuretics, antiplatelet agents, digoxin or GTN. Only systolic blood pressure and treatment with diuretics, digoxin and GTN retained significance in the multivariate model. This second model predicted attained exercise intensity more efficiently ($R = 0.677$). The standard error of the estimate is 1.810. Tables 4 and 5 present details of the models.

Age, BMI and sex were the most powerful predictors of exercise capacity in our model. We checked whether the other variables that we entered into our model (namely treatment with diuretics, GTN and digoxin, and systolic blood pressure) retained significance after controlling for these variables. Only blood pressure lost significance after controlling for the main determinants of exercise capacity.

To validate our model we tested our equation in an analysis of 87 consecutive patients with obesity and IHD. We used the simplest model that considered only age, BMI, sex and height.

Baseline characteristics were similar in the two groups with respect to all the variables considered in the equation; namely, age was 61.3 (8.5) years ($p = 0.237$ versus retrospectively analysed patients), BMI was 38.7 (5.4) kg/m^2 ($p = 0.072$) and height was 1.65 (0.09) m ($p = 0.868$). Twenty six (31%) were women ($p = 0.407$). Predicted exercise intensity was 6.3 (1.6) METs and attained was 6.3 (2.4) METs ($p = 0.903$); the difference between predicted and measured intensity was 0.03 (2.1) METs and the correlation coefficient between the two values was 0.534 ($p < 0.001$).

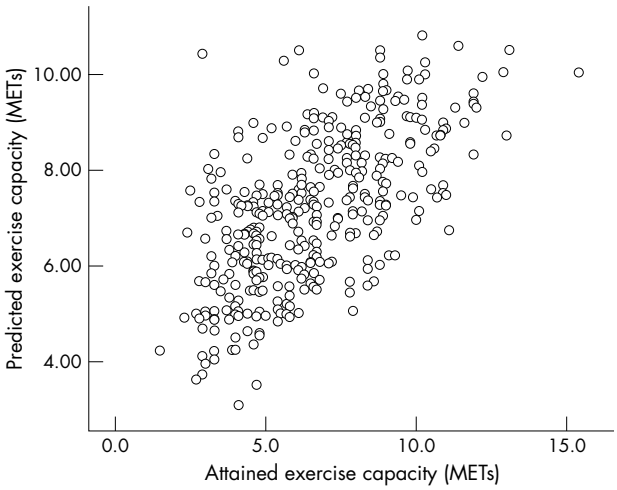

Figure 1 Predicted versus attained exercise capacity measured in metabolic equivalents (METs) and calculated as 14.53 – (0.12 × age (years)) – (0.17 × body mass index (kg/m^2)) + (3.16 × height (m)) (+ 0.71 for male patients).

Table 4 Multivariate linear model

Model	Variable	Unstandardised coefficient β	p Value
1	(Constant)	14.531	<0.001
	Age	−0.121	<0.001
	BMI	−0.168	<0.001
	Sex	0.711	0.018
	Height	3.158	0.039
2	(Constant)	13.933	<0.001
	Age	−0.106	<0.001
	BMI	−0.152	<0.001
	Sex	0.759	0.010
	Height	2.806	0.062
	Diuretic	−0.850	<0.001
3	(Constant)	14.030	<0.001
	Age	−0.101	<0.001
	BMI	−0.149	<0.001
	Sex	0.753	0.010
	Height	2.622	0.077
	Diuretic	−0.782	<0.001
	GTN	−0.684	0.002
4	(Constant)	13.534	<0.001
	Age	−0.100	<0.001
	BMI	−0.151	<0.001
	Sex	0.768	0.008
	Height	2.905	0.049
	Diuretic	−0.688	0.001
	GTN	−0.663	0.002
	Digoxin	−1.379	0.007
5	(Constant)	14.960	<0.001
	Age	−0.097	<0.001
	BMI	−0.146	<0.001
	Sex	0.751	0.009
	Height	2.758	0.060
	Diuretic	−0.671	0.001
	GTN	−0.714	0.001
	Digoxin	−1.488	0.004
	Systolic BP	−0.013	0.022

Exercise capacity (measured in metabolic equivalents) is the dependent variable. Age is measured in years, body mass index (BMI) is in kg/m^2, female sex = 0, male sex = 1, height is in m, treatment with a diuretic, glyceryl trinitrate (GTN) or digoxin is 0 if not treated and 1 if treated, and blood pressure (BP) is in mm Hg.

DISCUSSION

Our data show that the exercise capacity of obese patients with IHD may be predicted by a simple equation that takes into account anthropometric measures, age and sex. A small but significant power is added by diuretic treatment, GTN treatment, digoxin treatment and resting systolic blood pressure.

The determinants of exercise capacity are still poorly understood in the obese population and therefore it is not easy to predict the level of exercise that a patient will reach. Moreover, obese patients very rarely reach the levels of exercise tolerance that are considered normal (less than 20% in our study population).[22] We therefore need a new definition of exercise capacity that is tailored for obese people.

Even if the progression of age is the most important determinant of exercise tolerance, mainly because it determines a reduction in muscle mass and strength, we found that BMI is a highly significant determinant of the level of exercise. Obesity determines an increase in fatigue due to the high body mass that causes an increase in work for any given speed and inclination of the treadmill compared with

Table 5 Summary of the multivariate model

Model	Predictors	*R*	R^2	R^2 change	Residual SD
1	Age	0.469	0.220	0.220	
	Age, BMI	0.586	0.343	0.123	1.89
	Age, BMI, sex	0.624	0.390	0.047	
	Age, BMI, sex, height	0.630	0.397	0.007	
2	Age, BMI, sex, height, diuretic	0.650	0.423	0.026	1.85
3	Age, BMI, sex, height, diuretic, GTN	0.662	0.439	0.016	1.82
4	Age, BMI, sex, height, diuretic, GTN, digoxin	0.671	0.450	0.011	1.80
5	Age, BMI, sex, height, diuretic, GTN, digoxin, systolic BP	0.677	0.458	0.008	1.79

BMI, body mass index; BP, blood pressure; GTN, glyceryl trinitrate.

non-obese people. At any workload obese patients consume more oxygen than normal and therefore have reduced cardiorespiratory reserve. Myers and colleagues[13] found that BMI explained less than 2% of the variability of exercise capacity; however, they studied a population that was composed not only of obese participants but also of overweight, normal weight and possibly underweight patients. Enright and colleagues[25] found a non-linear relationship between BMI and exercise; nevertheless, if we consider only the obese subsets of patients in their study there is a linear negative relationship whereas BMI in the normal and overweight range seems to have little or no effect on the levels of exercise. In our series of patients waist circumference was not related to exercise capacity. Waist circumference loses its incremental predictive power in patients with BMI > 35 kg/m^2, which applies to over two thirds of our population.[26]

Sex is the third factor, in decreasing order of importance, that determines exercise capacity. Women exercise less than men probably because they have less muscle mass and a lower stroke volume. Lastly, height contributes less to the prediction of exercise capacity: we think that this may be due to a greater leg length conferring the ability to reach higher level of exercise for people of comparable BMI, age and sex.

Associated clinical conditions did not predict exercise tolerance in our population. Drug treatment, in contrast, gave a small but significant contribution; nonetheless, drug treatment may be considered to be a marker of associated clinical conditions. GTN, diuretics and digoxin use were all associated with a lower level of exercise. After age, sex and BMI were controlled for, each relationship retained significance indicating a true negative effect of treatment. More of the patients taking GTN had chest pain and had limited exercise intensity because of this symptom; we therefore believe that this may be the main reason for our finding. Even if diuretics and digoxin per se possibly influence exercise capacity negatively, patients with more severely reduced functional capacity may have been using those treatments. In our population, mainly the subset of patients with atrial fibrillation, used both diuretics and digoxin and therefore we can look at them as a marker of the presence of atrial fibrillation, which may be the true determinant of the loss of exercise capacity. Atrial fibrillation determines a loss of atrial systolic function as well as fast and irregular ventricular response. This reduces exercise tolerance especially in patients with reduced diastolic function such as those who are obese.[27] Treatment with β blockers was a significant univariate predictor of exercise capacity; the positive effect of β blockers, however, is not direct but is mediated through covariates. Indeed, treatment with β blockers in our series was negatively associated with age and BMI. As a consequence the relationship is no longer significant in the multivariate model.

The last variable that added power to our equation was systolic blood pressure, which may be looked at as a marker of fitness (the lower the pressure the better the fitness). Patients with poorly controlled hypertension after heart transplantation have a shorter exercise duration.[28] Nevertheless, the contribution if blood pressure to the model is low: when we controlled for BMI, age and sex the relationship between blood pressure and exercise intensity was no longer significant. Resting heart rate, which was one of the more significant univariate predictors of exercise capacity, did not add statistical power to the equation: heart rate was directly related to age and BMI and was higher in women. The significance was therefore lost when heart rate was considered in the multivariate model. As a general consideration, care must be taken in interpreting the univariate associations that we found, since many variables, besides being related to exercise capacity, were also related to age, BMI and sex and were not independent predictors of exercise tolerance.

One more issue deserves comment: in our series ejection fraction was not significantly related to exercise capacity. Enright *et al*[25] found no correlation between ejection fraction and distance walked in the six minute walk test, whereas Skaluba *et al*[29] found a strong correlation between ejection fraction and exercise duration with a Bruce protocol. Papers specifically reporting on obese patients are lacking. Overall our model explains nearly 50% of the variability of exercise tolerance and ejection fraction is only partially a descriptor of cardiovascular function: a thorough functional evaluation is necessary to understand the relationship between cardiac function and exercise capacity. The variance of exercise capacity that remains to be understood may be related to diastolic dysfunction,[29] which is almost invariably present in obese patients, and to other factors that are to be determined including left atrial function and a more accurate detection of systolic dysfunction.[30] Since our purpose was to describe a tool that can be used in everyday practice we did not consider diastolic function, which is not routinely assessed before exercise stress testing.

In our validation study we found a satisfactory correlation between predicted and measured exercise capacity: the model on average was very efficient in predicting attained intensity. Since our institution particularly serves patients with severe or complicated obesity who have very often faced multiple therapeutic failures, we have selected a population that is severely compromised. Even if our validation study was remarkably successful, before being introduced in clinical practice our equation has to be checked in different sets of patients, including those with non-complicated obesity, and following different exercise test protocols, taking care that the motivation of the patients during the test is standardised. Moreover, we point out that our equation has no value for overweight or normal weight patients. Follow-up studies are

needed to define the prognosis of patients who have a lower than predicted effort tolerance.

In conclusion, we have developed two different equations that may be used in clinical practice to predict the level of exercise of obese patients with IHD, therefore helping in the individualisation of exercise protocols and rehabilitation programs. Although the power of the second model is statistically superior, the difference is small and the agreement between the measured and predicted exercise intensity by our first equation can be judged to be satisfactory. We therefore believe that considering only age, sex, BMI and height suffices to give an acceptable estimate of exercise capacity of the individual patient.

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